Genetics Department, University of Wisconsin, Madison 6, Wis., Febr. 27, 1952

Dear Dr. Hayes:

Thank you for the reprints and your letter of the 20th. I am replying in haste, for I am going out of town presently; also, I hoped this might reach you in time for Cavalli's visit to London. Cavalli is, I think, very intimately acquainted with my views and, if he will, can speak for both of us on such questions as publication. I have proposed to him that since we have been collaborating as closely as the distance will permit we should publish fairly soon a full account of our work on self-incompatibility under an authorship such as Cavalli, Lederberg, and Lederberg.

There is very little doubt that we have been working on much the same thing, although my own interpretations are somewhat more conservative. It will help in the following discussion to symbolize the "infective" determinant of self-compatibility as F+. Such strains as W-677 and the SM- infertile strains that each of us seems to have picked up independently are then F-. This is referred to as self-incompatibility since F- x F- appeaas to be completely infertile. The transmission of F+ is quite unique, especially in its efficiency-- Cavalli can give you the details on this. I think your conclusion that recombination of other markers may be equally frequent is probably mistaken. In rather extensive tests, the only exchanges that were detected between well-marked F+ and F- involved F only, as far as could be detected without selective methods. The frequency for exchange of markers other than F is some 10^{-5} to 10^{-6} that of F+, or do you have some evidence to the contrary? (that is for the conditions under which the transmission of F has been studied). I think that a careful distinction should be made between the transmission of the F+ agent, whatever it is, and the transmission of "gametic" material.

As I wrote previously, I was not convinced that the different response of W-677 and of 58-161 to SM was pertinent to the sexual process itself, but thought it might be an irrelevant difference in sensitivity to streptomycin. As soon as I saw your paper in nature (1/19 issue), however, I tried the following experiment which obliges me to withdraw this reservation. We were aware, like yourself, that SM- F^+ S^S x TLB$_1$- F^- S^r (58-161 x W-1177) was moderately fertile on SM-minimal agar, while F^+ S^r x F^- S^S was not. If the difference were significant (in re sexuality) then one might expect that F^+ S^r would be fertile with F^+ S^S. Since W-677 could readily acquire F+ by transduction from K-12, the experiment could be done without any reasonable doubt that differences in streptomycin response per se would interfere. This proved to be correct: W-677F^+ was, in my first trial, fertile both with 58-161F^+S^r, and with F^-S^r also. I am obliged to admit, therefore, that your SM experiments have revealed a second function (may I call it G), such that a S^S is effectively G- in the presence of SM. For a dross, then, one parent must be G+, the other F+. I think it unneccassary to assume that an F+G+ cell can act only uniquely as a "gene donor" or acceptor. In a general way, the situation around F and G is symmetrical, and we cannot unequivocally assert the direction of transmission, if there is in fact a "direction" such as anisogamy. From a genetic point of view, in various F+ x F- crosses, the two parents are equivalent. I see no reason yet why we may not still be dealing with the union of morphologically equivalent elements, although the F-G setup does point to some degree of functional differentiation. To assume a microgamete when filtration experiments, or simple sedimentation, have given no evidence for it at all even in sensitive tests, calls, I think for Occam's razor, at least for public pronouncements. I say this more emphatically because of our experience with Salmonella transduction where the genetic and physical evidence point very much the other way (Spicer has a resume). I think I must not understand your hypothesis of the "self-reproducing gamete". What meiosis is it a product--in the haploid cell? It surely is not the F+ agent, which does not carry any other markers when transduced. I see nothing more infective about recombination in bacteria (i.e., in E. coli) than in the "parasitism" of any cell by its nucleus. F+ is a unique determinant for, as far as we know, a single trait: self-compatibility. Whether

this can be interpreted in terms of the capacity to produce a microgamete time will tell. But the gamete itself can no more be identified with the F+ agent than with lambda (as you seemed to imply in the Nature article).

Yours sincerely,

J. Lederberg